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EXAMINER	
MORRIS, PATRICIA L	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 11/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/786,556	VENKATRAMAN ET AL.	
	Examiner	Art Unit	
	Patricia L. Morris	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *11-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10, 26 and 27 are under consideration in this application.

Claims 11-25 are held withdrawn from consideration as being drawn to nonelected subject matter.

The restriction requirement is deemed sound and proper and is hereby maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-10, 26 and 27 are rejected under 35 U.S.C. 102(a), (b) and/or (e) as being anticipated by Takashi et al., Souda et al. and Reddy et al. for the reasons set forth in the previous Office action.

Again, Takashi et al., Souda et al. and Reddy et al. specifically disclose the instant rabeprazole sodium salt. Note example 33 of Souda et al. or the compound of formula 1 of Reddy et al. Hence, the instant compound is deemed anticipated therefrom.

Contra to applicants' arguments in the instant response, a novel chemical product is identified first by its "chemical nature", i.e. elemental and atom content. It is a well known fact that many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability

of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice. Thus in the strictest sense, polymorphs are different crystalline forms of the **same pure substance** in which the molecules have different arrangements and/or different conformations of the molecules. The term form Z does not offer any demarcation of the product from the prior art crystalline product.

Claim Rejections - 35 USC ∋ 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of in view of Takashi et al., Souda et al. and Nochi et al. in view of Haleblian et al., Brittain et al., Muzaffar et al. ,Jain et al., Chemical & Engineering News, US Pharmacopia, and Concise Encyclopedia Chemistry.

Again, Takashi et al., Souda et al. and Nochi et al. teach the crystalline form of rabeprazole and rabeprazole sodium as well as the pharmaceutical compositions. Note examples 32 and 33 and column 6, lines 5-9 of Souda et al. or the compound of formula 1 of Nochi et al. Brittain et ., Muzaffar et al., Jain et al. and Haleblian et al. teach that compounds can exist in different crystalline forms. Note, for example, page 60 of Muzaffar et al. Chemical & Engineering News, US Pharmacopia and Concise Encyclopedia teach that at any particular temperature and pressure, only one crystalline form is thermodynamically stable. Hence the claimed crystalline form as well as its relative selectivity of properties *vis-a-vis* the known compound are suggested by the references. It would appear obvious to one skilled in the art in view of the references that the instant compound would exist in different crystalline forms. Therefore, in the absence of unexpected results one skilled in the art in the possession of one polymorph would be expected to have polymeric crystalline forms for a drug and changing the form, purity or other characteristic of an old product does not render the novel form patentable where the difference in form purity or characteristic was inherent in or rendered obvious by the prior art. In re Cofer 148 USPQ 268.

Applicants appear to argue that one having ordinary skill in the art would not have been motivated to produce the compounds encompassed by the claims. The motivation is not abstract but is always related to the properties or uses that one having ordinary skill in the art would have expected the resulting compound to exhibit. In situations involving chemical compounds bearing a close similarity, the requisite motivation stems from the expectation that compounds exhibiting closely similar structures will exhibit similar properties. In the situation here, it is well known that instant compounds exist as polymorphs.

Applicants have supplied a reference to support their allegations that the instant polymorphs are not obvious from the prior art. Applicants are invited to note the reference where it is stated that polymorphs do in fact exist.

Claim Rejections - 35 USC ∋ 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants merely assert that this paragraph does not apply. This argument is clearly not persuasuive.

The specification is silent as to how the crystalline forms Z are produced. Further, it is recognized in the art that at a given temperature and pressure only one crystalline form is thermodynamically stable (see US Pharmacopia). The specification lacks description as to whether form Z are thermodynamically stable as to provide utility at room temperature for these forms and their compositions.

The specification disclose that the preparation of the instant polymorphs is conventional. However, different polymorphs cannot be produced by the same method. It is impossible to synthesize more than one metastable polymorphic form using the same method to synthesize the

different forms. At any given temperature and pressure, only one polymorph can be produced. Note, for example, page 873 of Concise Encylopedia Chemistry.

Again, there is a lack of description as to whether the compositions are able to maintain the compounds in the crystalline forms claimed. Processing a compound into a pharmaceutical composition could create a different form than the crystalline form being claimed or even back to the compound itself. See pages 912-913 of Habeblian. Doelker et al. Abstract, "One may also observe changes in technology or pharmaceutical properties that are due to polymorphic environmental conditions undergone by the product or dosage form." Taday et al. p 831...Once in the desired crystalline form, the polymorphic form may be changed by incorrect storage or even during tablet preparation" and p. 836, figure 8, wherein the compound form four in the pharmaceutical composition resulted in similar spectra. The specification fails to describe the pharmaceutical compositions claimed in terms of their X-ray diffraction pattern or infrared spectrum data. The X-ray diffraction and Infrared spectrum data in the specification only pertains to Forms X and Y of rabeprazole sodium rather than the compositions being claimed. Moreover, the specification fails to provide any X-ray diffraction and Infrared spectrum for the alleged hydrates of Forms X and Y and for their corresponding compositions.

Chemical & Engineering News disclose that formulation of drugs or pharmaceuticals in its metastable forms, for example, on polymorph, is highly unpredictable. The metastable forms will disappear and change into the most thermodynamically stable form. Muzaffar et al., p. 60 states "At any one temperature and pressure only one crystal form of a drug is stable and any other polymorph existing under these conditions will convert to the stable form." And p. 63-65 (a)-(h) pharmaceutical preparing processes affect polymorphism.

The specification lacks description of how the pharmaceutical compositions can be prepared in order to maintain the particular compound of a particular form with the particular infrared spectra and X-ray diffraction being claimed. Otsuka et al., p. 852 "..in formulation studies and the method preparing CBZ has been shown to affect the drug's pharmaceutical properties through the polymorphic phase transformation of the bulk CBZ powder during the manufacturing process." Disclosure of X-ray diffraction patterns for pharmaceutical compositions comprising the crystalline forms are lacking in the specification. The X-ray diffraction patterns in figure 1 and infrared spectra only supports the crystalline forms X and Y of rabeprazole sodium.

The specification has also not described how all the crystalline forms and compositions being claimed will be maintained and prevented from converting to other forms when used in the treatment of ulcers.

Applicants have provided no objective evidence that the instant form Z will not be identical to the prior art compound because "*when a crystalline solid is dissolved in solvent, the crystalline structure is lost so that different polymorphs of the same substance will show the same absorption spectra as solution"* (see Jain p. 316). Further, in the aqueous phase, *all physical forms are amorphous* (see Ulicky).

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement

and whether any necessary experimentation is undue. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention

The nature of the invention is the preparation of a novel crystalline forms Z of rabeprazole sodium and compositions.

State of the Prior Art

Polymorphs arise when molecules of a compound stack in the solid state in distinct ways. (See Chemical Engineering News, page 32). Although identical in chemical composition, crystalline forms can have very different properties. They are distinguishable by various analytical techniques, especially X-ray powder diffraction. Polymorphs tend to convert from less stable to more stable forms. No method exists to predict the polymorphs of a solid compound with any significant certainty. In drug design, it is best to work with the most stable polymorph, because it will not convert any further, however, the most stable polymorph usually is the least soluble. To improve bioavailability, drug companies sometimes trade off polymorph stability with solubility, choosing to work instead with the less stable forms first, also known as the metastable forms. Polymorphs can convert from one form to another during the manufacturing process of a pharmaceutical drug. See Chemical Engineering News, page 33. This is why it is

important to monitor the polymorph during manufacture of the drug to see if it persists during manufacture.

The amount of direction or guidance and the presence or absence of working examples

Figure 1 of the specification only disclose the X-ray diffraction pattern of one compound, i.e., Form Z of rabeprazole sodium in the crystalline form rather than the compositions being claimed in terms of the specific X-ray diffraction patterns. Polymorphs often change into other forms during drug manufacture into a pharmaceutical composition. Based on the unpredictability in the art, the applicant is not entitled to the X-ray diffraction patterns claimed for the compositions and pharmaceutical compositions.

Further, the specification fails to show that the instant polymorphs treat any ulcers. As evidenced by the art of record, it is well known that polymorphs can convert to the original compound.

The breadth of the claims

The breadth of the claim are drawn to the specific crystalline forms and in addition to the pharmaceutical compositions and processes of preparing.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the pharmaceuticals compositions being claimed and verifying that they have the specific X-ray diffraction patterns being claimed which are not disclosed in the specification. There is also lack of guidance as to whether the instant polymorphs rather than the original compound treats any ulcers.

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 26 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Again, claims 2-5, 26 and 27 lack antecedent basis for the recited limitations. Claim 1 does not permit the sodium forms or set forth the properties recited in the dependent claims. Claim 1 does not specify any X-ray powder diffraction patterns for in instant sodium forms.

Applicants merely cite a number of US patents in order to overcome the 112 rejections. The allowance of one application has no bearing at all on the instant application.

Again, the expression "substantially the same" in claim 4 is indefinite to its meaning. There is insufficient antecedent basis for the limitations.

The term Form Z in claims 1 and 7-10 is an universal identification of compounds. Further, the terms Crystal II, Form X and Form Y does not define specific compounds. What is meant by Crystall II?

Again, claims 1 and 6-10 contain the trademark/trade name rabeprazole. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a structure of a chemical compound and, accordingly, the identification/description is indefinite.

Further, the notation of Form Z of rabeprazole sodium is not an universal identification of compounds. Contra to applicants arguments, the term rabeprazole does not describe the chemical structure.

Again claims 4 and 26 are incomplete because the claims are not self-contained in particularly pointing out and distinctly claiming what applicants regard as their invention. This practice facilitates examination of the claimed invention by having the subject matter all in one place, avoids complicating the examination process by adding the processing of drawings and possible correction thereof, and permits the claimed subject matter to be easily modified without possible correction of drawings and potential modification of the scope of the disclosure as originally filed. Further, the public should not have to refer to the claimed subject matter in one place and not have to refer back and forth to at least two or three different places.

The claims measure the invention. United Carbon Co. V. Binney & Smith Co., 55 USPQ 381 at 384, col. 1, end of 1st paragraph, Supreme Court of the United States (1942).

The U.S. Court of Claims held to this standard in Lockheed Aircraft Corp. v. United States, 193 USPQ 449, The claims measure invention and resolution of invention must be based on what is claimed.

The C.C.P.A. in 1978 held that an invention is the subject matter defined by the claims submitted by the applicant. We have consistently held that no applicant should have limitations of the specification read into a claim where no express statement of the limitation is included in the claim. In re Priest, 199 USPQ 11, at 15.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10, 26 and 27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13, 26 and 27 of copending Application No. 10/786,556 in view of Haleblian et al., Muzzaffar et al., Jain et al., Chemical & Engineering News, US Pharmacopia, Brittain et al. and Concise Encyclopedia Chemistry.

This is a provisional obviousness-type double patenting rejection.

Again, Ser no. 10/505,826 discloses crystal forms of the instant salts and the corresponding compositions. The ancillary references teach that the mere existence of further polymorphs of compounds is not in itself regarded as unexpected. Hence, patentable distinction is not seen. Contra to applicants' arguments in the instant response, applicants have failed to show any unexpected or unobvious properties *vis-à-vis* the prior art compounds.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia L. Morris
Primary Examiner
Art Unit 1625

plm
November 16, 2005